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☐ 1: P00379. Dihydrofolate red...[gi:118974]

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LOCUS P00379 159 aa linear BCT 15-MAR-2004  
 DEFINITION Dihydrofolate reductase.  
 ACCESSION P00379  
 VERSION P00379 GI:118974  
 DBSOURCE swissprot: locus DYP\_ECOLI, accession P00379;  
 class: standard.  
 created: Jul 21, 1986.  
 sequence updated: Jul 21, 1986.  
 annotation updated: Mar 15, 2004.  
 xrefs: gi: [146005](#), gi: [146006](#), gi: [41264](#), gi: [41265](#), gi: [21321891](#),  
 gi: [21321929](#), gi: [1786230](#), gi: [1786233](#), gi: [26106314](#), gi: [26106368](#),  
 gi: [24050246](#), gi: [24050247](#), gi: [30039813](#), gi: [30039857](#), gi: [66098](#),  
 pdb accession 4DFR, gi: [231129](#), gi: [231205](#), gi: [231252](#), pdb  
 accession 1DRA, pdb accession 1DRB, pdb accession 2DRC, pdb  
 accession 3DRC, pdb accession 1DHI, pdb accession 1DHJ, pdb  
 accession 1DDR, pdb accession 1DDS, gi: [1942148](#), gi: [996100](#), pdb  
 accession 1DYH, pdb accession 1DYI, pdb accession 1DYJ, pdb  
 accession 1JOL, gi: [1943514](#), gi: [1942814](#), gi: [1942742](#), gi: [1942743](#),  
 gi: [1941993](#), gi: [1942744](#), pdb accession 1RB2, pdb accession 1RB3,  
 gi: [1942006](#), pdb accession 1RD7, pdb accession 1RE7, gi: [1942023](#),  
 gi: [1942024](#), gi: [1942025](#), gi: [1942605](#), gi: [1942541](#), gi: [1942542](#),  
 gi: [1942543](#), gi: [1942544](#), gi: [1942545](#), gi: [1942030](#), gi: [1942031](#),  
 gi: [2098461](#), pdb accession 1TDR  
 xrefs (non-sequence databases): SWISS-2DPAGEP00379,  
 ECO2DBASEB020.0, EcoGeneEG10326, InterProIPR001796, PfamPF00186,  
 PRINTSPR00070, PROSITEPS00075  
 KEYWORDS Oxidoreductase; NADP; Trimethoprim resistance; Methotrexate  
 resistance; One-carbon metabolism; 3D-structure; Complete proteome.  
 SOURCE Escherichia coli  
 ORGANISM Escherichia coli  
 Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales;  
 Enterobacteriaceae; Escherichia.  
 REFERENCE 1 (residues 1 to 159)  
 AUTHORS Smith,D.R. and Calvo,J.M.  
 TITLE Nucleotide sequence of the E coli gene coding for dihydrofolate  
 reductase  
 JOURNAL Nucleic Acids Res. 8 (10), 2255-2274 (1980)  
 MEDLINE [81053692](#)  
 PUBMED [6159575](#)  
 REMARK SEQUENCE FROM N.A.  
 SPECIES=E.coli; STRAIN=K12  
 REFERENCE 2 (residues 1 to 159)  
 AUTHORS Yura,T., Mori,H., Nagai,H., Nagata,T., Ishihama,A., Fujita,N.,  
 Isono,K., Mizobuchi,K. and Nakata,A.  
 TITLE Systematic sequencing of the Escherichia coli genome: analysis of  
 the 0-2.4 min region  
 JOURNAL Nucleic Acids Res. 20 (13), 3305-3308 (1992)  
 MEDLINE [92334977](#)  
 PUBMED [1630901](#)

REMARK SEQUENCE FROM N.A.  
SPECIES=E.coli; STRAIN=K12

REFERENCE 3 (residues 1 to 159)  
AUTHORS Blattner,F.R., Plunkett,G. III, Bloch,C.A., Perna,N.T., Burland,V.,  
Riley,M., Collado-Vides,J., Glasner,J.D., Rode,C.K., Mayhew,G.F.,  
Gregor,J., Davis,N.W., Kirkpatrick,H.A., Goeden,M.A., Rose,D.J.,  
Mau,B. and Shao,Y.  
TITLE The complete genome sequence of Escherichia coli K-12  
JOURNAL Science 277 (5331), 1453-1474 (1997)  
MEDLINE 97426617  
PUBMED 9278503

REMARK SEQUENCE FROM N.A.  
SPECIES=E.coli; STRAIN=K12 / MG1655

REFERENCE 4 (residues 1 to 159)  
AUTHORS Welch,R.A., Burland,V., Plunkett,G. III, Redford,P., Roesch,P.,  
Rasko,D., Buckles,E.L., Liou,S.-R., Boutin,A., Hackett,J.,  
Stroud,D., Mayhew,G.F., Rose,D.J., Zhou,S., Schwartz,D.C.,  
Perna,N.T., Mobley,H.L.T., Donnenberg,M.S. and Blattner,F.R.  
TITLE Extensive mosaic structure revealed by the complete genome sequence  
of uropathogenic Escherichia coli  
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 17020-17024 (2002)  
MEDLINE 22388234  
PUBMED 12471157

REMARK SEQUENCE FROM N.A.  
SPECIES=E.coli; STRAIN=06:H1 / CFT073 / ATCC 700928

REFERENCE 5 (residues 1 to 159)  
AUTHORS Stone,D., Phillips,A.W. and Burchall,J.J.  
TITLE The amino-acid sequence of the dihydrofolate reductase of a  
trimethoprim-resistant strain of Escherichia coli  
JOURNAL Eur. J. Biochem. 72 (3), 613-624 (1977)  
MEDLINE 77115802  
PUBMED 320005

REMARK SEQUENCE (ISOZYME 1).  
SPECIES=E.coli; STRAIN=B [RT500]

REFERENCE 6 (residues 1 to 159)  
AUTHORS Baccanari,D.P., Stone,D. and Kuyper,L.  
TITLE Effect of a single amino acid substitution on Escherichia coli  
dihydrofolate reductase catalysis and ligand binding  
JOURNAL J. Biol. Chem. 256 (4), 1738-1747 (1981)  
MEDLINE 81117257  
PUBMED 7007370

REMARK SEQUENCE (ISOZYME 2).  
SPECIES=E.coli; STRAIN=B [RT500]

REFERENCE 7 (residues 1 to 159)  
AUTHORS Bennett,C.D., Rodkey,J.A., Sondey,J.M. and Hirschmann,R.  
TITLE Dihydrofolate reductase: the amino acid sequence of the enzyme from  
a methotrexate-resistant mutant of Escherichia coli  
JOURNAL Biochemistry 17 (7), 1328-1337 (1978)  
MEDLINE 78187252  
PUBMED 350268

REMARK SEQUENCE.  
SPECIES=E.coli; STRAIN=B [MB1428]

REFERENCE 8 (residues 1 to 159)  
AUTHORS Flensburg,J. and Skold,O.  
TITLE Massive overproduction of dihydrofolate reductase in bacteria as a  
response to the use of trimethoprim  
JOURNAL Eur. J. Biochem. 162 (3), 473-476 (1987)  
MEDLINE 87161813  
PUBMED 3549289

REMARK SEQUENCE FROM N.A.

SPECIES=E.coli; STRAIN=1810

REFERENCE 9 (residues 1 to 159)

AUTHORS Jin,Q., Yuan,Z., Xu,J., Wang,Y., Shen,Y., Lu,W., Wang,J., Liu,H., Yang,J., Yang,F., Zhang,X., Zhang,J., Yang,G., Wu,H., Qu,D., Dong,J., Sun,L., Xue,Y., Zhao,A., Gao,Y., Zhu,J., Kan,B., Ding,K., Chen,S., Cheng,H., Yao,Z., He,B., Chen,R., Ma,D., Qiang,B., Wen,Y., Hou,Y. and Yu,J.

TITLE Genome sequence of *Shigella flexneri* 2a: insights into pathogenicity through comparison with genomes of *Escherichia coli* K12 and O157

JOURNAL Nucleic Acids Res. 30 (20), 4432-4441 (2002)

MEDLINE 22272406

PUBMED 12384590

REMARK SEQUENCE FROM N.A.  
SPECIES=S.flexneri; STRAIN=301 / Serotype 2a

REFERENCE 10 (residues 1 to 159)

AUTHORS Wei,J., Goldberg,M.B., Burland,V., Venkatesan,M.M., Deng,W., Fournier,G., Mayhew,G.F., Plunkett,G. III, Rose,D.J., Darling,A., Mau,B., Perna,N.T., Payne,S.M., Runyen-Janecky,L.J., Zhou,S., Schwartz,D.C. and Blattner,F.R.

TITLE Complete genome sequence and comparative genomics of *Shigella flexneri* serotype 2a strain 2457T

JOURNAL Infect. Immun. 71 (5), 2775-2786 (2003)

MEDLINE 22590274

PUBMED 12704152

REMARK SEQUENCE FROM N.A.  
SPECIES=S.flexneri; STRAIN=2457T / ATCC 700930 / Serotype 2a

REFERENCE 11 (residues 1 to 159)

AUTHORS Filman,D.J., Bolin,J.T., Matthews,D.A. and Kraut,J.

TITLE Crystal structures of *Escherichia coli* and *Lactobacillus casei* dihydrofolate reductase refined at 1.7 A resolution. II. Environment of bound NADPH and implications for catalysis

JOURNAL J. Biol. Chem. 257 (22), 13663-13672 (1982)

MEDLINE 83056868

PUBMED 6815179

REMARK X-RAY CRYSTALLOGRAPHY (1.7 ANGSTROMS).  
SPECIES=E.coli

REFERENCE 12 (residues 1 to 159)

AUTHORS Bystroff,C., Oatley,S.J. and Kraut,J.

TITLE Crystal structures of *Escherichia coli* dihydrofolate reductase: the NADP+ holoenzyme and the folate.NADP+ ternary complex. Substrate binding and a model for the transition state

JOURNAL Biochemistry 29 (13), 3263-3277 (1990)

MEDLINE 90241903

PUBMED 2185835

REMARK X-RAY CRYSTALLOGRAPHY.  
SPECIES=E.coli

REFERENCE 13 (residues 1 to 159)

AUTHORS Bystroff,C. and Kraut,J.

TITLE Crystal structure of unliganded *Escherichia coli* dihydrofolate reductase. Ligand-induced conformational changes and cooperativity in binding

JOURNAL Biochemistry 30 (8), 2227-2239 (1991)

MEDLINE 91152037

PUBMED 1998681

REMARK X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS).  
SPECIES=E.coli

COMMENT -----  
This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and

the EMBL outstation - the European Bioinformatics Institute.  
 The original entry is available from <http://www.expasy.ch/sprot>  
 and <http://www.ebi.ac.uk/sprot>

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 [CATALYTIC ACTIVITY] 5,6,7,8-tetrahydrofolate + NADP(+) =  
 7,8-dihydrofolate + NADPH.  
 [PATHWAY] Essential step for de novo glycine and purine synthesis,  
 DNA precursor synthesis, and for the conversion of dUMP to dTMP.  
 [MISCELLANEOUS] The strain K12 sequence is shown.  
 [MISCELLANEOUS] STRAIN B [RT500] IS RESISTANT TO 500 MICROGRAMS PER  
 MILLILITER OF TRIMETHOPRIM.  
 [MISCELLANEOUS] STRAIN B [MB1428] IS METHOTREXATE-RESISTANT.  
 [SIMILARITY] Belongs to the dihydrofolate reductase family.

FEATURES	Location/Qualifiers
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source	1..159 /organism="Escherichia coli O6" /db_xref="taxon:217992"
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gene	1..159 /gene="FOLA" /note="synonyms: TMRA, B0048, C0058, SF0045, S0047"
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<u>Region</u>	10..12 /gene="FOLA" /region_name="Helical region"
<u>Region</u>	13..15 /gene="FOLA" /region_name="Beta-strand region"
<u>Region</u>	25..35 /gene="FOLA" /region_name="Helical region"
<u>Region</u>	28 /gene="FOLA" /region_name="Variant" /note="L -> R (IN STRAIN B[RT500] ISOZYME 2)."
<u>Region</u>	30 /gene="FOLA" /region_name="Variant" /note="W -> G (IN STRAIN 1810)."
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<u>Region</u>	44..50 /gene="FOLA" /region_name="Helical region"
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Region      /gene="FOLA"
            /region_name="Variant"
            /note="E -> Q (IN STRAIN 1810)."
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ORIGIN

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121 gdthfpdyep ddwesvfsef hdadaqns hsycfeilerr
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Jan 20 2004 07:47:23